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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/220,920	12/24/98	MILBRANDT J	6029-7996

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HM12/0518

EXAMINER	
MERTZ,P	
ART UNIT	**PAPER NUMBER**
1646	8

DATE MAILED: 05/18/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/220,920	Milbrandt et al.
Examiner	**Group Art Unit**
Prema Mertz	1646

☒ Responsive to communication(s) filed on *Apr 3, 2000*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1, 11, 12, and 15-27* is/are pending in the application.

Of the above, claim(s) *1 and 11* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *12 and 15-27* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *5*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Election/Restriction

1. Applicant's election of Group II, claims 12, 15-27 in Paper No. 7 (4/3/00) is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 2-10, 13-14, 28-38 have been canceled previously. Claims 1, 11 are drawn to non-elected claims and claims 12, 15-27 are under consideration by the Examiner.

The amendment (Paper No.7, 4/3/00) and IDS (Paper No. 5, 3/5/99) have been entered.

Specification

2. A new title of the invention is required because the word "novel" is not considered as part of the title of an invention and the Patent and Trademark Office does not include such words at the beginning of the title of the invention. It is suggested that the word "novel" be deleted from the title of the invention. See MPEP § 606.01.

3. The Information Disclosure Statement filed in Paper No. 5 (3/5/99), fails to comply with the provisions of MPEP § 609 because of the form PTO-1449 or equivalent which was submitted or placed in the application file. Rule 37 CFR 1.98 specifies the contents of the Information Disclosure Statement, which includes a list of all patents, publications or other information submitted for consideration by the Office, a legible copy of each publication or that portion which cause it to be listed, and all other information or that portion which cause it to be listed. 37 CFR 1.98(b) requires that each publication must be identified by author (if any), title, relevant pages of the publication, date

and place of publication. The place of publication refers to name of the journal, magazine or other publication in which the information being submitted was published. To comply with this requirement, the list may not be incorporated into the specification but must be submitted in a separate paper. A separate list is required so that it is easy to confirm that applicants intend to submit an information disclosure statement and because it provides a readily available checklist for the Examiner to indicate which identified documents have been considered. Use of form PTO-1449, Information Disclosure Citation, is encouraged. Applicant is advised that the date of any re-submission of an item of information contained in a information disclosure statement or the submission of any missing element(s) is the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements. See MPEP § 609 C(1-2).

In this case, for the GenBank references (AF, AG, AI, AJ), the date of public availability of the sequences and the names of the authors, have not been cited.

Claim rejections-35 USC § 112, first paragraph

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4a. Claims 12, 15, 16, 19-23, 25-27, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description in this case only sets forth SEQ ID NO:6-8, 37-39, and equivalent degenerative codon sequences thereof and therefore the written description is not commensurate in scope with the claims drawn to conservatively substituted variants of the polypeptides encoded by the nucleic acid sequences set forth above, such variants resulting from conservative substitutions.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Reiger et al (Glossary of Genetics and Cytogenetics, Classical and Molecular, 4th Ed., Springer-Verlay, Berlin, 1976) clearly define alleles as one of two or more alternative forms of a gene occupying the same locus on a particular chromosome..... and differing from other alleles of that locus at one or more mutational sites (page 17). Thus, the structure of naturally occurring allelic sequences are not defined. With the exception of SEQ ID NO:6-8 and 37-39, the skilled artisan cannot envision the detailed structure of the encompassed polypeptide or the polynucleotide encoding

such and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Support for variants is provided in the specification on page 20, lines 3-32, page 21, lines 1-15, wherein it is disclosed that variants of the disclosed polypeptides may be naturally occurring variants or non-naturally occurring variants. However, no disclosure, beyond the mere mention of variants is made in the specification. This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Therefore only an isolated nucleic acid encoding polypeptides comprising the amino acid sequences of SEQ ID NO: 3-5, 34-36, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph. As a result, it does not appear that the inventors were in possession of nucleic acid molecules encoding variants of the polypeptide as recited in claims 12, 15, 16, 19-23, 25-27.

4b. Claim 21 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The deposit of the biological material is considered necessary for the enablement of the current invention (see M.P.E.P. Chapter 2400 and 37 C.F.R. §§ 1.801-1.809). Elements required for practicing a claimed invention must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. While applicants have disclosed that the plasmid has been deposited under the terms of the Budapest Treaty, the deposit number for the plasmid has not been provided on page 64 of the specification, and therefore, the specification is not compliant with all of the provisions for maintenance and availability of the deposited material. If the deposited material has been accepted for deposit under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure (e.g., see 961 OG 21, 1977), and Applicants, their assignee or their agent needs to provide a declaration containing the following: A statement that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of a patent.

A statement that the material has been deposited under conditions that assure that access to the material will be available during the pendancy of the patent application to one determined by the Commissioner to be entitled thereto under 37 C.F.R. 1.14 and 35 U.S.C. § 122.
A statement that the deposited material will be maintained with all of the care necessary to keep it viable and uncontaminated for a period of at least five years after the most recent request for the furnishing of a sample of the deposited microorganism, and in any case, for a period of at least thirty years after the date of deposit of for the enforceable life of the patent, whichever period is longer.
A statement by declarant that all statements made therein of declarant's knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the instant patent application or any patent issuing thereon.

4c. Claims 12, 15-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid encoding a protein comprising the amino acid sequence set forth in SEQ ID NO:3, 4, 5, 34, 35 or 36, does not reasonably provide enablement for a nucleic acid encoding "all" pan-growth factor proteins comprising artemin. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification delimits the instant nucleic acid encoding a protein by reference to specific amino acid arrays as set forth in SEQ ID NO:3, 4, 5, 34, 35, or 36, however, in the claims, the protein is defined by reference to the term "pan-growth factor", wherein the term itself does not represent any distinguishing information concerning the disclosed protein. Moreover because pan-growth factor does not inherently correspond to any particular protein, claims that lack the recitation of structural properties encompass subject matter not supported by the instant specification. Molecules

that are embraced by the claims are not adequately supported by the instant specification because the specification provides no guidance for how to make such molecules nor are examples provided as to how these molecules would be identified commensurate with the breadth of the claims. In the absence of an appropriate structural and/or functional reference, a person of ordinary skill in the art would be unable to make and use the molecules embraced by the claims without undue experimentation because one could not distinguish the nucleic acid molecules encoding proteins envisaged by the specification and those which are unrelated.

With respect to claims 12, 15-27, as recited, what is claimed in the instant invention broadly encompasses nucleic acid molecules encoding "all" pan-growth factor proteins. While the specification discloses that a "pan-growth factor" protein comprise a portion of artemin and a portion of at least one other growth factor from the TGF-β family (see page 7, lines 18-22), the specification is non-enabling for the unlimited number of nucleic acid compositions comprising pan-growth factor proteins, and which are encompassed by the scope of the claims. Claim 12 is a single means claim (M.P.E.P. 2164.08(a)). In In re Hyatt, 708 F.2d 712, 218 USPQ 195 (Fed. Cir. 1983), the Courts have held that: "A single means claim, i.e. where a means recitation does not appear in combination with another recited element of means, is subject to an undue breadth rejection under 35 U.S.C. 112, first paragraph." (A single means claim which covered every conceivable means for achieving the stated purpose was held nonenabling for the scope of the claim because the specification disclosed at most only those means known to the inventor). Since no material limitations for the nucleic acid encoding the protein have been recited in the claim and only a biological activity has been recited, the

claim encompasses every conceivable structure (means) for achieving the stated property (result), a fact situation comparable to Hyatt. The claimed invention encompasses compositions not envisioned or described in the specification, and neither does the specification disclose how these claimed compositions can be distinguished from each other. The specification only enables nucleic acid molecules encoding proteins having the amino acid sequences shown in SEQ ID NO: 3, 4, 5, or 34, 35, or 36, the polypeptides having specific characteristics and properties. These properties may differ structurally, chemically and physically from other known proteins. By application of the factors set forth in Ex parte Forman (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in In re Wands (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) quantity of experimentation, (2) guidance presented, (3) the predictability of the art, and (4) the breadth of the claims, in the instant application, the quantity of experimentation to determine which other nucleic acid molecules encoding proteins are encompassed by the scope of the claims is practically infinite and the guidance provided in the specification very little, thereby rendering the results of the assays taught in the specification unpredictable (see pages 54-62). Therefore, it would require undue experimentation to determine which nucleic acid molecules encoding proteins having the biological activity of a pan-growth factor protein, would be encompassed by the scope of the claims. The disclosure of six natural nucleic acid molecules encoding specific polypeptides is clearly insufficient support under the first paragraph of 35 U.S.C. § 112 for claims which encompass every and all nucleic acid molecules encoding pan-growth factor polypeptides, including mutants thereof. In In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), the Courts have held that:

"Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since some improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that the scope of the claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

Furthermore, the amount of embodiments corresponding to the desirable compositions, may be innumerable, and the enabled embodiments amount to only six. Therefore, there are substantial scientific reasons to doubt the scope of enablement, as set forth above. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. The specification does not describe any other nucleic acid molecules encoding polypeptides other than those whose amino acid sequences are shown in SEQ ID NO:3, 4, 5, 34, 35 and 36, and since it is deemed to constitute undue experimentation to determine all the others, the disclosure is not commensurate with the scope of the claims. Therefore, Applicants are not enabled for nucleic acid molecules encoding proteins having anything less than the amino acid sequences shown in SEQ ID NOS:3, 4, 5, 34, 35, 36. It is suggested that by employing conventional claim language, the claims be amended to include the specific nucleic acid molecules encoding polypeptides supported by the instant specification.

Claims 12, 15, and 25, each recite "fragment of...", which limitations are non-enabled by the specification in the absence of reference to a subset of amino acid sequences comprising the domains

to which the functional properties of the artemin polypeptides have been ascribed or for domains to which the functional properties of the polypeptides of the TGF-β superfamily have been ascribed. The specification provides no guidance as to which amino acids might comprise the minimum residues of a fragment which retains any enabled functional property peculiar to the instant polypeptides. One would not have a reasonable expectation of successfully making a representative number of nucleic acid fragments encoding amino acid fragments having biological activity consistent with the scope of the claims. Additionally, one would reasonably expect that fragmentation of the 113, 116, 140 amino acid residue polypeptides would abolish activity because activity is determined not only by primary sequence, but also by three-dimensional structure, as, for example, is the case for the ligand binding site of a receptor or for a catalytic site of an enzyme. Any arbitrary fragment of the amino acid sequence of SEQ ID NO:3, 4 or 5 would not be expected to confer the desirable protein activity. Therefore, in the absence of delimiting amino acid sequences that make up the functional domains of the instant nucleic acid molecules encoding proteins, a person of ordinary skill in the art would be unable to make fragments of the amino acid sequences or nucleic acid sequences embraced by the claims without undue experimentation to determine which fragments have biological activity.

4d. Claims 15-24, 26, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid molecule encoding a polypeptide set forth in SEQ ID NO:3, 4, 5, 34, 35 or 36 or a complement of said nucleic acid molecule, does not reasonably provide enablement for a nucleic acid molecule or a complement of a nucleic acid molecule encoding a polypeptide set forth in SEQ ID NO:3, 4, 5, 34, 35, or 36. The specification does not enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

With respect to claim 15, as recited, the claim encompasses a complement of a nucleic acid molecule encoding a polypeptide set forth in SEQ ID NO:3, 4, 5, 34, 35, or 36. The specification is non-enabling for a complement of a nucleic acid molecule encoding a polypeptide set forth in SEQ ID NO:3, 4, 5, 34, 35, or 36, because the specification does not provide the guidance to make a complement of a nucleic acid molecule that could encode a polypeptide having the amino acid sequence as set forth in SEQ ID NO:3, 4, 5, 34, 35, or 36. The instant specification is non-enabling for such, because how can one make a nucleic acid and a complement thereof, both encoding the same amino acid sequence. The specification provides no guidance and in the absence of such a disclosure, a skilled artisan would be unable to make/use the complement of a nucleic acid encoding a polypeptide set forth in SEQ ID NO:3, 4, 5, 34, 35, 36, as embraced by the claim. It is suggested that the claim be amended to recite "a nucleic acid molecule encoding a polypeptide set forth in SEQ ID NO:3, 4, 5, 34, 35, 36, or the complement thereof".

Claim rejections-35 USC § 112, second paragraph

5. Claims 12, 16-18, 23, 25, 26, are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 is unclear because it cannot be determined if the fragment of at least 8 contiguous amino acids belongs to the artemin amino acid sequence or for the pan-growth factor.

Similarly with respect to claim 25 it cannot be determined if the fragment of at least 8 contiguous amino acids belongs to the artemin polypeptides recited.

Claim 23, line 5, is incorrect because SEQ ID NO:42 is a nucleotide not an amino acid sequence.

Claim 16, line 6 recites "hybridizes to a mature human artemin nucleotide sequence", the recitation of "hybridizes" being a relative and conditional term and renders the claim indefinite. Furthermore, some nucleic acids which might hybridize under conditions of moderate stringency, for example, would fail to hybridize at all under conditions of high stringency. The metes and bounds of the claims thus cannot be ascertained. This rejection could be obviated by supplying specific conditions supported by the specification which Applicants consider to be "stringent". Furthermore, the recitation of "mature" is incorrect because the nucleotide sequence is not "mature" but encodes a mature human artemin protein.

Claim 26 is incorrect because it recites "artemin antisense oligonucleotide" rather than an antisense oligonucleotide which is complementary to the nucleic acid encoding artemin as set forth in SEQ ID NO:3, 4, 5, 34, 35, 36. Furthermore, claim 26, is also improper because it is dependent on claim 15 which recites that the nucleic acid encodes artemin, but an antisense nucleotide cannot encode the same protein as a sense nucleotide. It is suggested that this claim be rewritten independently of the sense nucleotide claim.

Claims 17-18 are rejected as unclear insofar as they depend on claim 16 for its limitations.

Claim rejections-35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6a. Claims 12, 15-16, are rejected under 35 U.S.C. § 102(a) as being anticipated by Waterston (1998).

Waterston disclose a cDNA isolated from humans (AC005038). A copy of the comparison of SEQ ID NO:6 claimed in the instant invention and the cDNA disclosed in the reference is enclosed at the end of this action (SEQUENCE COMPARISON A). The cDNA of the reference would be capable of hybridizing under low stringency conditions, to the polynucleotide of SEQ ID NO:6 described in the instant application. Therefore, the cDNA sequence disclosed in the reference meets the limitations of a nucleic acid molecule which specifically hybridizes to the nucleotide sequence set forth in SEQ ID NO:6.

Claim rejections-35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 19, 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Waterston et al (1998).

The disclosure of Waterston has been set forth above in paragraph 6. Claims 19-20 differ from the claims above in that the claimed DNA is placed in an expression vector and host cell which expresses the putative protein encoded thereby. To have incorporated the recombinant DNA identified by Waterston, into an expression vector and host cell to facilitate the production and characterization of the protein encoded thereby by employing those methods that were old and well known in the art of molecular biology at the time that the instant invention was made would have been prima facie obvious to an artisan in light of the Waterston publication.

Conclusion

No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (703) 308-4229. The examiner can normally be reached on Monday-Friday from 8:00AM to 4:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4227. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Prema Mertz

Prema Mertz Ph.D.
Primary Examiner
Art Unit 1646
May 8, 2000

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Db   1366 GTGGACCGCCTCTCCGCCACCGCCTGCGGCTGCCTGGGCTGA 1407


RESULT   4
AF120274
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KEYWORDS    .
SOURCE      human.
  ORGANISM  Homo sapiens
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REFERENCE   1  (bases 1 to 1892)
  AUTHORS   Hansen,C., Blom,N. and Johansen,T.E.
  TITLE     Neublastin a novel member of the GDNF ligand family
  JOURNAL   Unpublished
REFERENCE   2  (bases 1 to 1892)
  AUTHORS   Hansen,C., Blom,N. and Johansen,T.E.
  TITLE     Direct Submission
  JOURNAL   Submitted (14-JAN-1999) Cellular biology, NeuroSearch A/S,
            Smedeland 26B, Glostrup DK-2600, Denmark
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BASE COUNT      295 a    710 c    598 g    289 t
ORIGIN


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  Best Local Similarity  100.0%;  Pred. No. 2.2e-39;
  Matches  342;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 gctgggggcccgggcagccgcgctcgggcagcgggggcgcggggctgccgcctgcgctcg 60
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ACCESSION   AC005038
VERSION     AC005038.1  GI:3212953
KEYWORDS    HTG; HTGS_PHASE1.
SOURCE      human.
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Mammalia;
            Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 190728)
  AUTHORS   Waterston,R.H.
  TITLE     The sequence of Homo sapiens clone
  JOURNAL   Unpublished
REFERENCE   2  (bases 1 to 190728)
  AUTHORS   Waterston,R.H.
  TITLE     Direct Submission
  JOURNAL   Submitted (12-JUN-1998) Genome Sequencing Center, Washington
            University School of Medicine, 4444 Forest Park Parkway, St. Louis,
            MO 63108, USA
COMMENT     * NOTE: This is a 'working draft' sequence. It currently
            * consists of 5 contigs. The true order of the pieces
            * is not known and their order in this sequence record is
            * arbitrary. Gaps between the contigs are represented as
            * runs of N, but the exact sizes of the gaps are unknown.
            * This record will be updated with the finished sequence
            * as soon as it is available and the accession number will
            * be preserved.
            *        1    13034: contig of 13034 bp in length
            *    13035    13052: gap of unknown length
            *    13053    25068: contig of 12016 bp in length
            *    25069    25086: gap of unknown length
            *    25087    64951: contig of 39865 bp in length
            *    64952    64969: gap of unknown length
            *    64970   104799: contig of 39830 bp in length
            *   104800   104817: gap of unknown length
            *   104818   190728: contig of 85911 bp in length.
FEATURES             Location/Qualifiers
     source          1. .190728
                     /organism="Homo sapiens"
                     /db_xref="taxon:9606"
                     /clone="NH0486I22"
BASE COUNT    47737 a  48496 c  48872 g  45551 t     72 others
ORIGIN


  Query Match           85.4%;  Score 292;  DB 33;  Length 190728;
  Best Local Similarity  96.8%;  Pred. No. 3.9e-33;
  Matches  331;  Conservative    0;  Mismatches    5;  Indels    6;  Gaps    3;

Qy      1 gctgggggcccgggcagccgcgctcgggcagcgggggcgcggggctgccgcctgcgctcg 60
          |||||||| |||||||| |||||||||||||||||||||||| ||||||||||||
Db  67799 GCTGGGGGGCCGGGCAG-CGCGCTCGGGCAGCGGGGGCGCGGGGCTG-CGCCTGCGCTCG 67742

Qy     61 cagctggtgccggtgcgcgcgctcggcctgggccaccgctccgacgagctggtgcgtttc 120
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db  67741 CAGCTGGTGCCGGTGCGCGCGCTCGGCCTGGGCCACCGCTCCGACGAGCTGGTGCGTTTC 67682

Qy    121 cgcttctgcagcggctcctgccgccgcgcgcgctctccacacgacctcagcctggccagc 180
          ||||||||||||     || |  | ||||||||||||||||||||||||||||||||||
Db  67681 CGCTTCTGCAGCG----CTCCTCCGGCGCGCGCTCTCCACACGACCTCAGCCTGGCCAGC 67626

Qy    181 ctactgggcgccggggccctgcgaccgccccgggctcccggcccgtcagccagccctgc 240
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Db  67625 CTACTGGGCGCCGGGGCCCTGCGACCGCCCCCGGGCTCCCGGCCCGTCAGCCAGCCCTGC 67566

Qy    241 tgccgacccacgcgctacgaagcggtctccttcatggacgtcaacagcacctggagaacc 300
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Db  67565 TGCCGACCCACGCGCTACGAAGCGGTCTCCTTCATGGACGTCAACAGCACCTGGAGAACC 67506

Qy    301 gtggaccgcctctccgccaccgcctgcggctgcctgggctga 342
          |||||||||||||||||||||||||||||||||||||||||||
Db  67505 GTGGACCGCCTCTCCGCCACCGCCTGCGGCTGCCTGGGCTGA 67464


RESULT   6
AC005051/c
LOCUS       AC005051   132698 bp    DNA             HTG       12-JUN-1998
DEFINITION  Homo sapiens clone RG037F03, *** SEQUENCING IN PROGRESS ***, 12
            unordered pieces.
ACCESSION   AC005051
VERSION     AC005051.1  GI:3212940
KEYWORDS    HTG; HTGS_PHASE1.
SOURCE      human.
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Mammalia;
            Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 132698)
  AUTHORS   Waterston,R.H.
  TITLE     The sequence of Homo sapiens clone
  JOURNAL   Unpublished
REFERENCE   2  (bases 1 to 132698)
  AUTHORS   Waterston,R.H.
  TITLE     Direct Submission
  JOURNAL   Submitted (12-JUN-1998) Genome Sequencing Center, Washington
            University School of Medicine, 4444 Forest Park Parkway, St. Louis,
            MO 63108, USA
COMMENT     * NOTE: This is a 'working draft' sequence. It currently
            * consists of 12 contigs. The true order of the pieces
            * is not known and their order in this sequence record is
            * arbitrary. Gaps between the contigs are represented as
            * runs of N, but the exact sizes of the gaps are unknown.
            * This record will be updated with the finished sequence
            * as soon as it is available and the accession number will
            * be preserved.
            *        1     1483: contig of 1483 bp in length
            *     1484     1500: gap of unknown length
            *     1501     3489: contig of 1989 bp in length
            *     3490     3506: gap of unknown length
            *     3507     5674: contig of 2168 bp in length
            *     5675     5691: gap of unknown length
            *     5692    10331: contig of 4640 bp in length
            *    10332    10348: gap of unknown length
            *    10349    15810: contig of 5462 bp in length
            *    15811    15827: gap of unknown length
            *    15828    20876: contig of 5049 bp in length
            *    20877    20893: gap of unknown length
            *    20894    26544: contig of 5651 bp in length
            *    26545    26561: gap of unknown length
            *    26562    35813: contig of 9252 bp in length
            *    35814    35830: gap of unknown length
            *    35831    45222: contig of 9392 bp in length
            *    45223    45239: gap of unknown length
            *    45240    60183: contig of 14944 bp in length
            *    60184    60200: gap of unknown length
            *    60201    77865: contig of 17665 bp in length
            *    77866    77882: gap of unknown length
            *    77883   132698: contig of 54816 bp in length.
FEATURES             Location/Qualifiers
     source          1. .132698
                     /organism="Homo sapiens"
                     /db_xref="taxon:9606"
                     /clone="RG037F03"
BASE COUNT    34236 a  31999 c  33721 g  32555 t    187 others
ORIGIN


  Query Match           79.1%;  Score 270.4;  DB 33;  Length 132698;
  Best Local Similarity  96.5%;  Pred. No. 4.3e-30;
  Matches  330;  Conservative    0;  Mismatches    6;  Indels    6;  Gaps    5;

Qy      1 gctgggggcccgggcagccgcgctcgggcagcgggggcgcggggctgccgcctgcgctcg 60
          ||||||||||||||||||||||||||||||||||||||  ||  |||||  |||||||||
Db 113700 GCTGGGGGCCCGGGCAGCCGCGCTCGGGCAGCGGGGGCGGCGGCGTGCCG-CTGCGCTCG 113642

Qy     61 cagctggtgccggtgcgcgcgctcggcctgggccaccgctccgacgagctggtgcgtttc 120
          |||||||||||||||||||||||||||||||||||||||||||||||||||  | ||
Db 113641 CAGCTGGTGCCGGTGCGCGCGCTCGGCCTGGGCCACCGCTCCGACGAGCTGGT--GGTTT 113584

Qy    121 cgcttctgcagcggctcctgccgccgcgcgcgctctccacacgacctcagcctggccagc 180
          |||||||||| |||||||||| ||||||||||||||||||||||||||||||||||||||
Db 113583 CGCTTCTGCA-CGGCTCCTGCCG-CGCGCGCGCTCTCCACACGACCTCAGCCTGGCCAGC 113526

Qy    181 ctactgggcgccggggccctgcgaccgccccgggctcccggcccgtcagccagccctgc 240
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Db 113525 CTACTGGGCGCCGGGGCCCTGCGACCGCCCCCGGGCTCCCGGCCCGTCAGCCAGCCCTGC 113466

Qy    241 tgccgacccacgcgctacgaagcggtctccttcatggacgtcaacagcacctggagaacc 300
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Db 113465 TGCCGACCCACGCGCTACGAAGCGGTCTCCTTCATGGACGTCAACAGCACCTGGAGAACC 113406

Qy    301 gtggaccgcctctccgccaccgcctgcggctgcctgggctga 342
          |||||||||||||||||||||||| ||||||||||||||||
Db 113405 GTGGACCGCCTCTCCGCCACCGCCTGC-GCTGCCTGGGCTGA 113365


RESULT   7
AF109402
LOCUS       AF109402      675 bp    mRNA            ROD       30-DEC-1998
DEFINITION  Mus musculus neurotrophic factor artemin precursor (Artn) mRNA,
            complete cds.
ACCESSION   AF109402
VERSION     AF109402.1  GI:4071354
KEYWORDS
SOURCE      house mouse.
  ORGANISM  Mus musculus
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Mammalia;
            Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
REFERENCE   1  (bases 1 to 675)
  AUTHORS   Baloh,R.H., Tansey,M.G., Lampe,P.A., Fahrner,T.J., Enomoto,H.,
            Simburger,K.S., Leitner,M.L., Araki,T., Johnson,E.M. Jr. and
            Milbrandt,J.
  TITLE     Artemin, a novel member of the GDNF ligand family, supports
            peripheral and central neurons and signals through the
            GFRalpha3-RET receptor complex
  JOURNAL   Neuron 21 (6), 1291-1302 (1998)
  MEDLINE   99098192
REFERENCE   2  (bases 1 to 675)
  AUTHORS   Baloh,R.H., Fahrner,T.J. and Milbrandt,J.
  TITLE     Direct Submission
  JOURNAL   Submitted (25-NOV-1998) Pathology, Washington University, 660 S.
            Euclid Ave, St. Louis, MO 63110, USA
FEATURES             Location/Qualifiers
     source          1. .675
                     /organism="Mus musculus"
                     /db_xref="taxon:10090"
     gene            1. .675
                     /gene="Artn"
     CDS             1. .675
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                     /note="glial cell line-derived neurotrophic factor ligand
                     family member"
                     /codon_start=1
                     /product="neurotrophic factor artemin precursor"
                     /protein_id="AAC98691.1"
                     /db_xref="GI:4071355"
                     /translation="MELGLAEPTALSHCLRPRWQSAWWPTLAVLALLSCVTEASLDPM
                     SRSPAARDGPSPVLAPPTDHLPGGHTAHLCSERTLRPPPQSPQPAPPPPGPALQSPPA
                     ALRGARAARAGTRSSRARTTDARGCRLRSQLVPVSALGLGHSSDELIRFRFCSGSCRR
                     ARSQHDLSLASLLGAGALRSPPGSRPISQPCCRPTRYEAVSFMDVNSTWRTVDHLSAT
                     ACGCLG"
     mat_peptide     334. .672
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                     /product="neurotrophic factor artemin"
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